REMARKS

Claims 46-74 are pending in the present application. Claims 69-74 have been withdrawn from consideration due to a restriction requirement. Claim 46 has been amended to recite "active pharmaceutical ingredient" corresponding to the abbreviation "API" and to clarify that the pharmaceutical composition is formulated in a form for oral administration. Aside from the obvious context provided by claim 1 itself and the remaining claims (with respect to properties in gastric media), support for this amendment is found at, for example, paragraph [0073], [0093], and [0297] of the published application. No claims are added or canceled.

It is noted that, while the Office Action describes claim 46-68 as rejected, no basis is given for the rejection of claims 50-51 (claims 50-51 have not been included in the rejection under 35 U.S.C. § 103). Applicants request clarification in the next Office Action, in a non-final context, so that such claims may be properly addressed if subject to rejection.

Rejection under 35 U.S.C. § 103(a)

Claims 46-49 and 52-57 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Arora, *et al.* (U.S. Patent Application 2004/0029946) (hereinafter "*Arora*") in view of Carter (US Patent 6,613790) (hereinafter "*Carter*"). Applicants respectfully traverse as the claimed invention is not disclosed or suggested by the cited references.

The present invention is directed toward orally administered pharmaceutical compositions having preferred delivery profiles "wherein the composition retards crystallization or precipitation of the API for at least 5 minutes in gastric fluid conditions." Although the claims' recitation of gastric fluid conditions and the retardation of crystallization or precipitation of the API for at least 5 minutes in gastric fluid conditions as well as the bioavailability of the orally administered compositions (e.g. claims 60-62) makes clear that the claims are in the context of oral administration, the present amendment makes oral administration explicit.

In contrast, Arora concerns itself exclusively with *topical* applications of COX-2 inhibitors, including celecoxib, driven in part, because of the known problems in reproducibly administering COX-2 inhibitors orally (for example, Arora at paragraph [0002] states: "[topical administration] bypasses the portal circulation and thereby the hepatic first-

pass metabolism, avoids the variable systemic absorption and metabolism and also, potentially reduces gastro-intestinal irritation associated with oral administration"). Indeed, the reason that Arora does not teach that the salt form of celecoxib has an aqueous solubility less than about 10 mg/mL in gastric fluid conditions is because Arora does not contemplate the oral administration of its compositions. Further, to the extent that Arora discloses the use of polaxomers with COX-2 inhibitors, these polaxomers are provided as gelling agents for making topical creams (Arora at paragraph [0025]), not as precipitation retardants in oral formulations.

In acknowledging that Arora does not teach that the salt form of celecoxib has an aqueous solubility less than about 10 mg/mL in gastric fluid conditions or the specific salt forms listed in claims 58-59, the Examiner cites Carter as teaching pharmaceutically acceptable salts of COX-2 inhibitors, including celecoxib. Although Carter does describe an oral administration of the drugs (see Carter at col. 44, lines 40-46), Carter describes preferred methods of administration as parenterally, intravenously, or intramuscularly (Carter at col. 17, lines 15-19), and provides no relevant formulary teaching for oral administration. In particular, Carter does not teach the use of polaxomers or any other precipitation retardant, a sufficient deficiency in view of the pending claims.

Moreover, even combining the cited references would not result in the claimed invention. For example, incorporation of the salts of Carter into the formulations of Arora would still provide a topical formulation, as opposed to the claimed orally administered composition. And to the extent that Carter teaches the possibility of using its compounds as oral medicaments, the cited references provide no teaching of, or direction to use, a topical gellant for retarding crystallization or precipitation in gastric fluid conditions.

In view of the above, Applicants request reconsideration and withdrawal of the § 103 rejection.

Conclusion

Applicants believe that the foregoing constitutes a complete and full response to the Office Action of record. Accordingly, an indication of allowability of all pending claims is respectfully requested.

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